PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 58072 PCT (47137)	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/26125	International filing date *(day/month/year)* 20 August 2003 (20.08.2003)	Priority date *(day/month/year)* 21 August 2002 (21.08.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 15/89; C12M 3/00 and US Cl.: 435/29,287.1		
Applicant COLLECTRICON AB		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22 March 2004 (22.03.2004)	16 March 2005 (16.03.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer William H. Beisner Telephone No. 571-272-1700

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/26125

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-41 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 42-50, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-15, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Inventive Step (IS)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Industrial Applicability (IA)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 25, 35, 58 and 59 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 23, 35 and 59 are indefinite for the following reason(s): With respect to claim 25, "the cell chamber" lacks antecedent basis. Note claim 25 depends from claim 9 not claim 24. With respect to claim 35, "the housing" lacks antecedent basis. Note claim 35 depends from claim 32 not claim 34. With respect to claims 58 and 59, "the cell-contacting surface" lacks antecedent basis. Note claims 58 and 59 depend from claim 34 not claim 56.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V.1. Reasoned Statements:
The opinion as to Novelty was positive (Yes)with respect to claims 7, 8, 19, 22, 26, 30, 33, 34, 36, 37, 40, 46-48, 50-54, 57-62, 71-73, 75, 85, 86
The opinion as to Novelty was negative (No) with respect to claims 1-6, 9-18, 20, 21, 23-25, 27, 28, 31, 32, 35, 38, 39, 41-45, 49, 55, 56, 63-70, 74, 76, 78-84
The opinion as to Inventive Step was positive (Yes)with respect to claims NONE
The opinion as to Inventive Step was negative(NO) with respect to claims 1-86
The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-86
The opinion as to Industrial Applicability was negative(NO) with respect to claims NONE

V. 2. Citations and Explanations:

Claims 1-6, 9-18, 20, 21, 23-25, 27, 28, 31, 32, 35, 38, 39, 41-45, 49, 55, 56, 63-70, 74, 76 and 78-84 lack novelty under PCT Article 33(2) as being anticipated by Baumann et al. With respect to claim 1, the reference of Baumann et al. discloses a substantially planar substrate (4) with at least one conducting element (6) wherein the substrate includes at least one nonplanar element (20) for establishing and/or maintaining electrical communication with a cell (3). With respect to claims 2 and 3, see hollow element (16, 38). With respect to claims 4 and 5, nonplanar element (20) includes conducting (32) and nonconducting (9) surfaces. With respect to claim 6, see column 13, lines 1-5. With respect to claims 9-12, 27 and 28, see element 38 and column 16, lines 28-67. With respect to claims 13-20 and 23, the see nonplanar element (20/38) which is integral with substrate (4) and meets the structure of a capillary. With respect to claims 24 and 25, see Figure 17 and column 16, line 61, to column 17, line 2. With respect to claim 31, see Figure 22 and related text. With respect to claim 32, see element (6). With respect to claim 35, the see nonplanar element (20/38) which is integral with substrate (4) and meets the structure of a capillary. With respect to claim 38, see electrode 15. With respect to claim 39, see elements (20,6). With respect to claims 41-45 and 49, see Figure 17 and column 16, line 61, to column 17, line 2. With respect to claim 55, see, nonplanar element (20) includes conducting (32) and nonconducting (9) surfaces. With respect to claim 56, see element 38 and column 16, lines 28-67. With respect to claims 63-70, see discussion of previous claims above. The method of using the device disclosed in the reference of Baumann et al. meets the method steps recited in claims 74, 76 and 78-84.

Claims 7, 8, 22, 26, 29, 30, 36, 61, 71-73 and 75 lack an inventive step under PCT Article 33(3) as being obvious over Baumann et al. The reference of Baumann et al. has been discussed above. Claims 7, 8 and 36 differ by reciting specific materials of construction. For example the electrode is made of carbon and the substrate is made of an elastomer polymer. However, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum material of construction using art recognized materials such as carbon and elastomer polymers while maintaining the efficiency of the cell recording device. With respect to the surface treatments of claims 26, 28, 30 and 71-72, it would have been obvious to one of ordinary skill in the art to treat the surfaces for cell adhesion to render them hydrophilic while rendering non-cell adhesion surfaces hydrophobic. Such treating steps are notorious in the art and can include chemical washing and/or chemical deposition with respect to an existing material. With respect to claims 22, 61 and 75, while the reference of Baumann et al. discloses an insulator resistance of greater than 10Mohms, the instant claims require a resistance of at least 100Mohms. However, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to optimize the insulator resistance based on design considerations such as the materials of construction and/or the cells to be employed in the device while maintaining the efficiency of the system.

Claims 19, 33, 34, 37, 40, 46-48, 50-55, 57-60, 62, 77, 85 and 86 lack an inventive step under PCT Article 33(3) as being obvious over Baumann et al. in view of Stett et al.(WO 02/03058). The reference of Baumann et al. has been discussed above. With respect to claim 19, 33 and 40, these claims differ by reciting that the non-planar element is movable or removable from the planar substrate.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

The reference of Stett et al. discloses that it is known in the art to construct a non-planar element for contacting a cell that is movable or removable (See Figures 3-5). In view of this teaching, it would have been obvious to one of ordinary skill in the art to make the non-planar element of the primary reference so as to be removable for the known and expected result of providing a means recognized in the art for changing a cell contacting member such that the rest of the device can be reused. With respect to the use of an electrode within a lumen of claims 34, 37, 58 and 59, the reference of Stett et al. discloses that use of a lumen with an electrode is a known means recognized in the art for measuring cell membrane potential (See Figure 4, elements 23, 41 and 43). In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ an electrode/electrolyte construction as suggested by the reference of Stett et al. in the system of the primary reference for the known and expected result of providing an alternative means recognized in the art to achieve the same result. With respect to the cell delivery and flow limitations of claims 46, 47, 50-54, 60, 77, 85 and 86, the reference of Stett et al. discloses that it is known in the art to provide a cell chamber for immobilization of cells for recording cell membrane potential with a flow system for introducing cells (See Figures 1 and 2) and/or reagents into the cell chamber for immobilization of cells relative to a recording site. In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the system of the primary reference with a cell and reagent contacting system as suggested by the reference of Stett et al. for the known and expected result of providing a means known in the art for introducing cells and/or reagents relative to cell membrane potential recording sites. With respect to the use of micropositioning devices of claims 48, 57 and 62, the reference of Stett et al. also discloses the use of micropositioning devices to further aid in the manipulation of cells relative to a recording site. Their use in the system of the primary reference would have been obvious for the known and expected result of aiding in the positioning of the cells relative to the cell membrane recording sites.

Claims 1-86 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

---------- NEW CITATIONS ----------

WO 02/03058 A2 (STETT et al.) 10 January 2002 (10.01.2002), see entire document, especially Figures 1-5.